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# FACTORS INFLUENCING ANTIEPILEPTIC DRUG NON-COMPLIANCE IN EPILEPTIC PATIENTS OF PAKISTAN

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## ABSTRACT

Failure to comply with drug regimes is prevalent amongst patients with epilepsy and the consequence of this is often an increased risk of further seizures and other associated harms including increased health care costs. Contributing factors leading to non-compliance of anti-epileptic drugs has not been examined in Pakistan. We investigated the factors influencing non-compliance to prescribed antiepileptic drugs (AEDs). A cross-sectional study was employed for a total of 53 epileptic patients with non-compliance of anti-epileptic drugs. The data-collection tools were a questionnaire and structured interview for this study. Results showed that males were more liable to non-compliance of AEDs as compared to females. Medication complexity (more than 2 antiepileptic drugs), treatment duration (>6 months) and elderly age (> 55 years) were the major reasons of non-compliance. Further implementation of educational programmes for people with epilepsy would help to improve levels of compliance thereby reducing the risk of unnecessary seizures.

**Key words:** Epilepsy, Antiepileptic drugs, Non-compliance factors, Pakistan

## Introduction:

Epilepsy is a common and widespread neurological disorder, affecting people of all ages and socioeconomic classes worldwide.<sup>1</sup> Of those diagnosed with epilepsy, the vast majority of such patients are advised with antiepileptic drugs (AEDs) and approximately 70% may become seizure-free once the most effective regime is followed.<sup>2</sup> However, approximately every third of patients with epilepsy continue to experience seizures despite the prescription of appropriate doses of AEDs.<sup>3</sup> Poor compliance to AEDs may be the most important cause of poorly controlled epilepsy. The term "compliance" describes the extent to which a patient takes medications, as prescribed with respect to dosage and dosing intervals.<sup>4</sup> Non-compliance to treatment is widespread especially for chronic disease and is considered to be a significant problem faced by medical practice. Failing to comply increases the likelihood of hospital admissions, thus there could be a potential saving to the health care services if compliance could be improved. The term non-compliance lists following aspects in its definition: not taking the correct dosage (too much or too little), failing to leave the recommended length of time between doses, not taking medication for the duration specified, taking other drugs not prescribed. Some physicians believe that any patient who fails to adhere on one occasion or

more is non-compliant whereas others feel that only those who fail to comply more than occasionally, say at least 25% of the time, should be classed as non-compliant.<sup>5</sup> Non-compliance to AEDs by epileptic patients has been reported to be high and studies have demonstrated a higher prevalence of seizures (21-45%) in those who did not comply to their AED regimens.<sup>6,7</sup> In addition, non-compliance to AEDs has been reported to increase morbidity and mortality, as well as decrease quality of life and productivity.<sup>9</sup> Non-compliance was also reported to be associated with reduced mental and emotional wellbeing, including impaired cognition. Of the world's 50 million people with epilepsy, 85% live in developing countries.<sup>1</sup> However, few studies on compliance have been performed in Asian and developing countries.<sup>5</sup> However, none of those was conducted in Pakistan in order to determine prevalence of non-compliance and factors which lead to non-compliance of AEDs in epileptic patients. We therefore conducted this study on a sample of adult patients with epilepsy to examine major factors associated with non-compliance to AEDs.

## Materials and Methods

The cross-sectional study was conducted in OPD (Outpatient Department) at Services Institute of Medical Sciences and

Services Hospital, Lahore, Pakistan. Male and female patients, aged 10 to 70 years, who had been diagnosed with epilepsy at least one year previously, were included in this 6-month study which was originally conducted in 1st July- 30th December 2012. Patients who met the following criteria were also invited to participate in this study: (1) therapy recommended with at least one AED, irrespective of any standard or non-standard treatment; (2) suspected or reported non-compliance to AEDs and (3) no change in AEDs in the last six months. Patients with comorbidities (Diabetes, Ischemic heart disease) and those who were not able to respond to an interview were excluded. In this study, we included a total of 225 patients who were having the primary diagnosis of Epilepsy. This number was calculated statistically with help of software after taking 95% confidence interval and 5% absolute precision. Out of these 225, 53 patients were reported to be non-compliance to AEDs. A total of 53 patients reported with non-compliance to AEDs were included in the present study. The patients were arbitrarily divided into three age groups: an adolescent group (10-30 years), an adult group (31-55 years), and an older group (56-70 years). The data-collection tools were a questionnaire which was completed through structured interview. The patient survey comprised questions regarding demographics (gender, age, etc.), seizure history (type and frequency), current AED treatments, self-reported non-compliance to AEDs, and the reasons of non-compliance. The questionnaires were completed in the presence of parents for children patients (< 15 years of age). For this study, compliance was defined as not missing a dose and non-compliance as missing a dose or stopping treatment in the last month. The socio-economic status of the patients' parents was determined using variables like area of residence and monthly income. In this way, the subjects were categorized into Low class if they had a monthly income < 15,000 PKR; Middle class if monthly income was between 15,000-30,000; and High class if income was > 30,000. Participants gave written informed consent after the purpose of the study had been explained to them. The ethics committee of the hospital approved the study.

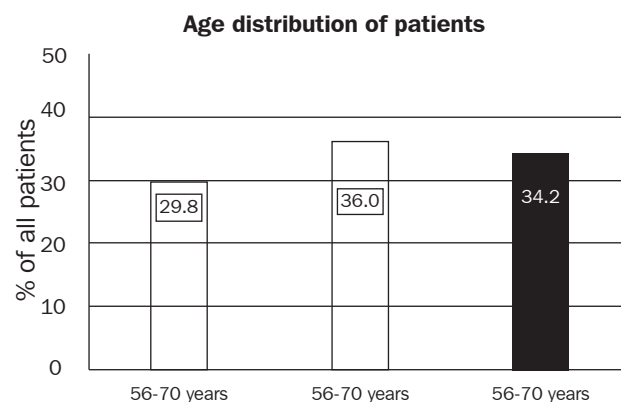
## Statistical analyses

The descriptive statistical analysis included examinations of means, standard deviations, frequencies, ranges, and percentages. The statistical packages SPSS (Version 20) and MS Excel (MS Office 2010) were used.

## Results

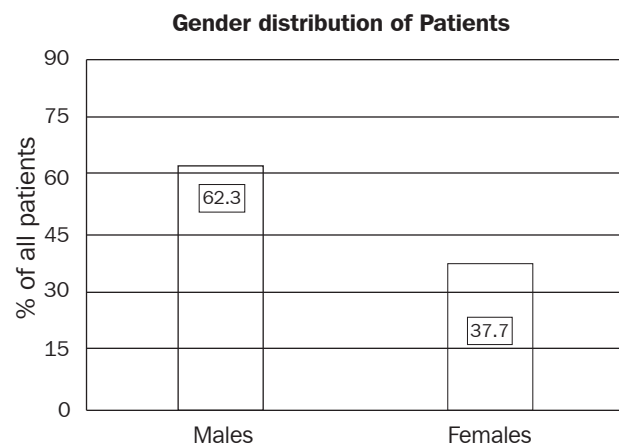
In total, 53 patients met all study inclusion criteria, and who

agreed to participate in the study. The patients came from different cities and towns of Lahore division. When epileptic patients reported with non-compliance were divided into three age groups, adult patients (31-55 years) represented the largest age group (36% of all patients) followed by old patients (34%) and adolescents (30%) (Figure 1).



**Figure 1.** Age distribution of epileptic patients reported with non-compliance of AEDs.

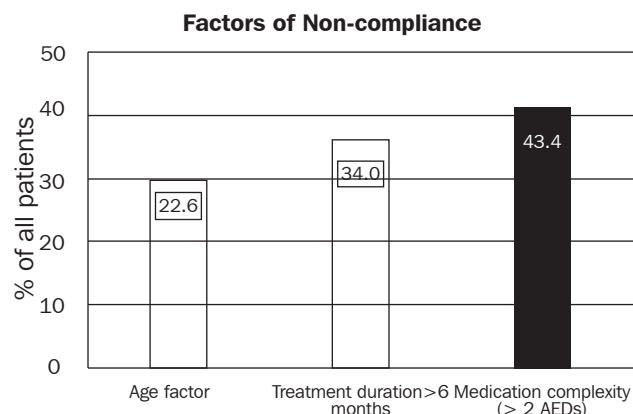
Of all patients with non-compliance, 33 (62.3%) were males and 20 (37.7%) were females. The mean patient age ( $\pm$ SD) was 46.9 ( $\pm$ 5.3) years (range: 10-70 years) (Figure 2).



**Figure 2.** Gender distribution of epileptic patients reported with non-compliance of AEDs.

Three main factors were identified in this study which led to non-compliance of AEDs in all 53 patients. Age factor, Treatment duration and medication complexity were the main reasons of non-compliance. Of the all the patients, the primary reason was medication complexity. A total of 43.4% patients did not comply to the AEDs treatment when the physician advised more than two AEDs. This was the major reason of non-compliance. Treatment duration was the second largest

reason attributing the patients towards non-compliance. Of all the patients, 34% reported that they could not comply because of treatment duration. Treatment duration greater than 6 months was cut-off period beyond which there was significant non-compliance to AEDs. Third reason of non-compliance was age factor as it was reported by 22.6% of the patients. Figure 1 clearly shows that non-compliance was less frequent in younger population as it shows only 29% of the patients. Elderly people specifically aged more than 31-55 years and 55-70 years could not comply to AEDs.



**Figure 3.** Frequency of factors contributing towards non-compliance of AEDs in Epileptic patients

Socio-economic (education status, economic class) and psychosocial factors like Beliefs (myths), Motivation, Attitude of the patients were strongly correlated with the non-compliance AEDs. Economic class of the patients was made on the basis of monthly income, type of profession and area of residence of the patients. On this basis, patients were classified into Low class (monthly income < 15000), Middle Class (monthly income up to 25000) and High class (monthly income > 25000). Table 1 shows that non-compliance behavior was presented mainly by patients belonging to low (35%) and middle class (47%). Similarly non-compliance of AEDs was greater in patients with lower education as 47% of the patients were having only primary education. Another factor was the marital status of the patients. Table 1 clearly shows that

among all the patients of non-compliance, almost 68% were single and only 32% were married.

## Discussion

This is the one of the first studies which was carried out to investigate the related factors of non-compliance to AEDs in epilepsy patients in Pakistan. Compliance is difficult to measure accurately. For epilepsy, compliance to medication has previously been measured by self-reporting, drug blood level monitoring, and prescription refill monitoring. Compliance measured by self-reporting may be overestimated but is considered to be the simplest and least expensive method. In this study, major reasons of non-compliance were measured by self-reporting. In our study, 23% of patients were non-compliant to AEDs. This percentage was smaller than that reported in other countries: Arab countries (64%), the United States (29-58%), and the United Kingdom (59%).<sup>5,9,10</sup> In our study, elderly patients aged more than 55 years had the highest rates of non-compliance. This may be due to the fact that elderly patients have more difficulty in following instructions due to cognitive impairment or other physical difficulties, such as problems in swallowing tablets, opening drug containers, handling small tablets, distinguishing colours or identifying markings on drugs.<sup>11</sup> The duration of treatment period was also a factor that affected non-compliance. In a study of epilepsy patients, omission of dose was reported to be more frequent with a longer duration of seizure medication use.<sup>7</sup> The long treatment duration might compromise patients' beliefs about medication effectiveness. In our study, the one of three factors that affected compliance was the duration of treatment period. There were many factors that influenced patients' perception and beliefs with regards to non-compliance because of longer duration of treatment. Patients' knowledge about their disease and treatment is not always adequate and they may lack an understanding of the role of therapy, be fearful of dependency on long-term medication, lack knowledge about the disease and consequences of non-compliance, and may assume that the need for medication is intermittent and thus stop taking the drug in order to see whether medication is still required.<sup>12,13</sup>

Economic Class (%)			Marital Status (%)		Psycho-social factor (%)		Educational level (%)				Forgetfulness (%)	
Low	Middle	High	Single	Married	Yes	No	Illiterate	Elementary	Matric	Intermediate	Yes	No
35	47	18	67.9	32.1	68	32	15.1	47.2	20.8	17	49.2	50.8

**Table 1.** Socio-economic and individual factors attributing to non-compliance AEDs in Epileptic patients.

For these reasons, patient education is very important in order to enhance compliance. A poor patient-prescriber relationship is another strong factor which affects patient compliance; good relationship may enhance compliance. In order to build a healthy relationship, physicians should not only question patients about seizure frequency and current medication use, but also specifically probe them about compliance. They should give patients a detailed explanation about the disease, treatment regimens, the true side effects, and the importance of compliance, and spend more time with the patients.<sup>13</sup>

## Conclusion

Medication compliance remains an important issue in epilepsy treatment especially in developing countries. The non-compliance of epilepsy patients is common in Pakistan as well. Medication complexity (more than 2 antiepileptic drugs), treatment duration (>6 months) and elderly age (> 55 years) were major reasons of non-compliance. Targeted management programs and communication strategies are necessary to improve compliance to antiepileptic drug treatment for patients with epilepsy and avoid the clinical consequences of poor compliance.

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### Author's contribution:

**Dr. Safia Bano :** Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review

**Dr. Ahsan Numan :** Study concept and design, data analysis, manuscript writing, manuscript review